



What is a DMOAD?

TECHNICAL BULLETIN

KEY POINTS

Introduction

Overview:

Canine osteoarthritis (OA)

What is a DMOAD?

What are the requirements for approval?

Highlight:

Key Facts About OA

What is the clinical significance of a DMOAD?

Conclusion

Introduction

Osteoarthritis (OA), also known as degenerative joint disease (DJD), is the most common cause of chronic pain in dogs.¹ While OA is not life-threatening, its progression can seriously impact a dog's mobility and overall quality of life.

Traditionally, management of osteoarthritis has been viewed as an age-related issue focused on reducing clinical signs and relieving pain without treating the cause. Ideally, what's needed is a proactive solution that can alleviate symptoms and modify the course of the disease to reduce and slow its progression.

One such solution is a disease-modifying osteoarthritis drug (DMOAD) to reduce the loss of articular cartilage, slow the progression of joint structural damage, and promote healthy joint component maintenance.

While there is a high level of interest in the potential of a DMOAD throughout the veterinary industry, there is also a need to know more about them. Most dog owners, even some veterinarians, have never heard of DMOADs. In addition, many are unaware of the distinct and proven differences between a disease-modifying osteoarthritis drug compared to a symptom-modifying therapy for OA.

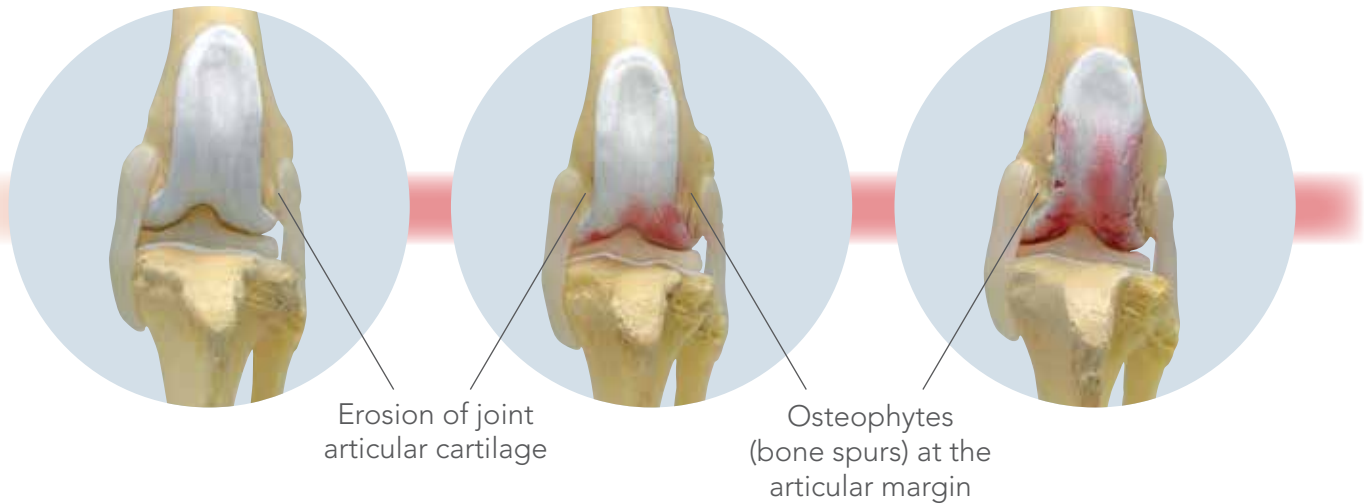
The purpose of this technical bulletin is to help answer some of the most relevant questions about DMOADs, including:

- How they're defined
- Clinical implications and potential for treatment of OA
- Regulatory requirements

Since DMOADs may have the ability to help manage the disease and improve the outlook for dogs with OA, it's worth learning more.

CANINE STIFLE WITH PROGRESSIVE DAMAGE

PROGRESSION OF DEGENERATIVE JOINT DISEASE



Images GPI Anatomicals

Overview: Canine osteoarthritis (OA)

Mobility is essential to a healthy life, and yet osteoarthritis affects nearly a quarter of the canine population.² To fully understand a DMOAD, it's logical to review the basics of the disease it targets. OA is a painful disease caused by deterioration of a joint's cartilage, surrounding tissue and fluid.¹ Over time, this can lead to bone-on-bone contact, chronic inflammation, swelling — and an increasingly painful life for a dog.¹

Joints are complex structures; for them to perform effectively, they must remain stable. Instability exerts abnormal forces on a joint, which results in erosion of articular cartilage and a cycle of progressive damage.

The unique and complex structure of articular cartilage gives it a limited capacity for intrinsic healing and repair. Articular cartilage is a highly specialized connective tissue of synovial joints. Unlike most tissues, it contains no blood vessels, lymphatics or nerves. It is, however, subjected to the harsh biomechanical environment, the daily "wear and tear" of every movement.

Once articular cartilage wears away completely, it can't be restored so it's vital to help maintain key articular cartilage components. Special diets, supplements and anti-inflammatory drugs can play a role in managing symptoms of joint disease but none of them specifically address the degradation of cartilage from OA.

What is a DMOAD?

While there is not yet one official, universally accepted definition, in essence, a disease-modifying osteoarthritis drug (DMOAD) is a pharmaceutical that's capable of making a positive impact on altering or reducing the progression of osteoarthritis.

In a recently published abstract, experts concur and further explain that a DMOAD is

“...a drug that modifies the underlying OA pathophysiology and potentially inhibits the structural damage to prevent or reduce long-term disability with potential symptomatic relief.”³

Descriptions may vary but experts and researchers appear to agree on certain factors that set DMOADs apart from other products designed to treat OA.

These include the ability to:

- Slow the progression of osteoarthritis
- Decrease joint inflammation
- Alleviate or reduce joint pain
- Reduce joint damage from progression of OA
- Improve joint health

What are the requirements for approval?

Regulatory agencies for both veterinary and human drugs, as well as academic scientists, members of regulatory authorities and representatives from the pharmaceutical industry, have also weighed in with recommendations to determine what defines a DMOAD.

Regulatory guidance from the Food and Drug Administration (FDA) suggests acceptance of structural endpoints for the development of products for the treatment of OA should be based on either “empirical evidence from randomized, controlled comparisons of clinical trials and/or based on a comprehensive understanding of the disease process and product mechanism of action, that an effect on the candidate structural endpoint will reliably predict an effect on the clinical outcomes of interest.”⁴

In the 2018 “Guidance for Industry,” the FDA provided its thinking on considerations of a DMOAD.

“The ultimate goal of treatments related to inhibition of structural damage or targeting the underlying pathophysiology associated with OA is to avoid or significantly delay the complications of joint failure...and also to reduce the deterioration of function and worsening pain.”⁴

Beyond demonstration of a significant difference when compared to a placebo, a primary consideration for approval as a disease-modifying osteoarthritis drug is evidence of improvement in clinical outcomes.

There are numerous ways to evaluate the stages of osteoarthritis and the effects of treatment. One, known as joint space narrowing (JSN), focuses on the severity of OA by measuring the space between bones in the joint; the less space, the more advanced the OA.⁵ Another is the Canine Osteoarthritis Staging Tool (COAST),⁷ which helps veterinarians and their clients evaluate the stages of OA to guide treatment and monitor the disease as it progresses.

What is the clinical significance of a DMOAD?

According to the American College of Veterinary Surgeons, treatment recommendations for OA are multimodal. This means they incorporate different approaches and can be either conservative, surgical or a combination of approaches including weight control, activity modification, rehabilitation, pain control, joint supplements and a disease-modifying drug (DMOAD).

As veterinarians determine which choice of pharmaceuticals, nutraceuticals and supplements are most appropriate for their canine OA patients, there are two broad categories to consider:

- **Symptom-modifying drugs or nutritional supplements** are used to reduce the clinical signs of osteoarthritis. Generally, these may alleviate some of the most common clinical signs (such as pain and inflammation) but they do not affect the progression of the disease.
- **Structure-modifying or disease-modifying drugs (DMOADs)** are capable of slowing, stabilizing, even repairing, the progression of osteoarthritis and the damage it causes to joints.

The key take-away here is that while symptom-modifying drugs, nutraceuticals or supplements may alleviate clinical signs they do not slow the progression of OA.

The distinct value of a DMOAD is that it can help slow the progression of the OA disease, help to repair damage, and promote improved joint health and mobility.

It’s important for veterinarians to note that a DMOAD designation from the FDA requires the submission and approval of efficacy data before making product claims. Other products, such as nutraceuticals, are not subject to regulatory mandates so the claims they make may be based on limited research or data.⁶

In comparison, **a DMOAD is clinically proven** to modify the disease. As an FDA-approved pharmaceutical, a DMOAD is also required to be prescribed by a licensed veterinarian, which helps to assure the most accurate dosing, safe use and appropriate monitoring.

KEY FACTS ABOUT OA

Contributing Factors ⁷	Joints Most Affected ⁷	Four Stages ⁷
<ul style="list-style-type: none"> • Developmental Orthopedic Disease • Genetics • Age • Excess Bodyweight • Gender • Exercise • Diet 	<ul style="list-style-type: none"> • Hip • Stifle • Elbow 	<p>Stage 1 Pre-osteoarthritis Injuries or developmental problems are more likely to affect a dog's joints.</p> <p>Stage 2 Signs include less interest in going on walks and playing.</p> <p>Stage 3 Signs include limping, struggling to get up, lie down or refusing to climb stairs.</p> <p>Stage 4 The dog loses the ability to walk or function. Signs are always visible.</p>

While the stages of osteoarthritis are universal, dogs progress through these stages at variable rates.



Conclusion

TECHNICAL BULLETIN

References

1. 2016 NAVC Proceedings, Osteoarthritis in Dogs and Cats: Novel Therapeutic Advances, M Epstein, DVM, DABVP C/F, CVPP; K Kirkby Shaw, DVM, MS, PhD, DACVS, DACVSMR.
2. "Osteoarthritis In Dogs," American College of Veterinary Surgeons, <https://www.acvs.org/small-animal/osteoarthritis-in-dogs>, accessed Feb. 9, 2020.
3. "Disease modification in osteoarthritis: are we there yet?" W.M. Oo, D.J. Hunter, Clin Exp Rheumatol 2019; 37 (Suppl. 12): S135-S140
4. "Osteoarthritis: Structural Endpoints for the Development of Drugs, Devices, and Biological Products for Treatment Guidance for Industry," U.S. Department of Health and Human Services, Food and Drug Administration. August 2018.
5. "Classifications in Brief, Kellgren-Lawrence Classification of Osteoarthritis," M.D. Kohn, BA, A.A. Sassoon, MD, N.D. Fernando, MD, Clin Orthop Relat Res (2016) 474:1886-1893
6. "Outcome Assessment In Clinical Trials Involving Medical Management Of Osteoarthritis In Small Animals," S.C. Budsberg, DVM; Osteoarthritis, 0195-5616/97.
7. Face validity of a proposed tool for staging canine osteoarthritis: Canine Osteoarthritis Staging Tool (COAST), T. Cachon, O. Frykman, J.F. Innes, B.D.X. Lascelles, M. Okumura, P. Sousa, F. Staffieri, P.V. Steagall, B. Van Ryssen, COAST Development Group, The Veterinary Journal, 235 (2018) 1-8.
8. E. Mele, Epidemiology of Osteoarthritis. Veterinary Focus 17, 4-10 (2007).

Conclusion

Osteoarthritis and degenerative joint disease is not, as once believed, just an age-related condition. Dogs of all ages can develop OA, and it continues to be an ongoing challenge for veterinarians as they strive to treat and manage the disease. Since damage to cartilage is associated with significant musculoskeletal disease, maintaining the health of articular cartilage is paramount to joint health.

Looking for early signs of a problem can help to proactively identify and address canine OA and or degenerative joint disease early in the process.

Allowing the functional and structural changes associated with canine OA to occur is doing a great disservice to the patient. The joint degradation of OA is incurable, and early intervention to disrupt the progressive cycle of the multidimensional joint deterioration is the most effective way to manage OA.⁷

Currently, greater than 50 percent of canine arthritis cases are diagnosed in dogs between 8–13 years of age.⁸ And, even though advancing age, increasing bodyweight and obesity contribute to the progression and severity of OA, this high percentage of older age diagnosis is a concern, given the known link between OA and the developmental of orthopedic disease in younger dogs.⁷

“While there is no simple cure that erases OA, several strategies make a significant positive impact on the progression and effects of OA,” according to Denis J. Marcellin-Little, DEDV, DACVS, DACVSMR. Proactive OA management is more effective because maintaining strength is much easier than recovering it. ”

FDA guidance supports a proactive approach as well, emphasizing the need for treatments to inhibit the structural damage or target the underlying pathophysiology of OA to reduce pain and slow the complications of joint damage, deterioration and failure.⁴

Hence, the real value of a DMOAD for dogs with OA (and their families), is that it may be a way to proactively reduce damage, slow progression of the disease, and effectively change their lives.